No sex difference in mouse digit ratio: reply to Voracek

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Voracek specializes in the study of human non-neural morphology (Voracek & Fisher 2002) and suicide (Voracek 2005), and he does not appear to appreciate the methods used in experimental mouse genetics. We (Bailey et al. 2005) investigated 2D:4D digit ratio in inbred mouse strains, because the findings can lead directly and fruitfully to a genetic analysis of factors that lead to higher and lower ratios (we follow the convention of using 2D:4D to refer to this digit ratio as have all previous published animal and human studies of hind limb digit ratios. We know of no published work using Voracek's 2T:4T nomenclature. A PubMed search over the past 5 years uncovered not one paper using 2T:4T but 135 using 2D:4D, including all seven investigating hind limb digits). Indeed, our study detected substantial and interesting strain differences, although significant sex differences were not found. Voracek is evidently disappointed at the lack of a sex difference in our data and seeks to dismiss them by branding our work a 'pilot study' whose results 'diverge from other mouse evidence'.

The sum total of the 'mouse evidence' for the genus *Mus* is three studies. Brown et al. (2002) measured left and right hind paws of 32 weanling and 39 adult 'outbred lab mice' of unspecified origin, and they found a significantly lower 2D:4D ratio for males than females only for the right paw. Manning et al. (2003) measured only the left hind paw for 111 mice of unspecified age and strain. The poorly specified genetic composition of the two populations is appalling. Manning et al. did not even replicate the finding of Brown et al. for the right paw; hence, it is difficult to see how our data for a larger sample of 175 inbred mice from eight well-defined and easily replicable strains could 'diverge' from those two. Furthermore, for three strains with lower average digit ratios (BALB/cByJ, BTBR/T + tf/J and C3H/HeJ), we did find a lower ratio for males than females, although the sex difference was too small to achieve significance. While differences in measurement techniques (see discussion in Bailey et al. 2005) prevent rigorous comparisons of ratio values across studies, note that the absolute values from the Manning et al. study are almost exactly the same as the absolute values and sex differences of the C3H/HeJ strain in our study.

Voracek suggests that the evidence supporting a correlation between finger length ratio and developmental androgen exposure is very strong. We regard the evidence as circumstantial but suggestive. The Lutchmaya et al. (2004) study found a correlation between testosterone : estradiol and 2D:4D ratios in a small, combined sample of 18 males and 15 females. Differences in 2D:4D between human ethnic groups dwarf differences between the sexes, and sex differences also vary considerably across ethnic groups (Manning et al. 2000; McFadden et al. 2005). This suggests that the testosterone exposure story is at least an over-simplification. The only experimental study that manipulated developmental testosterone was Romano et al. (2005), which produced a change in hind limb digit ratio in pheasants.

More data are needed to illuminate the true relationship between developmental variables and digit ratio. For example, it would be interesting to study an F2 hybrid population, because extreme inbreeding might disrupt the regulation of developmental processes involving the digits. For the average effect size of the sex difference that

we observed (d = 0.04), the research would need to be done with samples of at least 5000 per sex to achieve power of 90% when using Type I error probability = 0.05 (Wahlsten 1991).

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